**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of: James L. Brown
Serial No.: 09/539,735 Group No.: P. Nolan
Filed: 03/30/00 Examiner: 1644
Entitled: **DIAGNOSIS OF AUTOIMMUNE DISEASE**

# DECLARATION UNDER 37 C.F.R. § 1.132 BY JAMES L. BROWN

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

**CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)(1)(i)(A)**

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

Dated: 5-12-04 By: _____

Sir:

1. I, James L. Brown, am inventor of the subject matter claimed in the instant application, and I am the subject of the Curriculum Vitae and author of the publications shown on the list attached thereto. On the basis of the information and facts contained in those documents, I submit that I am qualified to speak on the level of ordinary skill in the art of the claimed invention.

2. The Examiner rejected Claims 1, 3-16 and 18-33 for alleged obviousness over Evans *et al.*[1] in view of Yamashiro *et al.*,[2] arguing that the levels of cAMP generation were "directly correlated" to the level of gene expression detection by a luminometer.

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1 Evans *et al.* (1999) "Development of a luminescent bioassay for thyroid stimulating antibodies," J. Clin. Endocrin. Metabolism 84(1)374-377.

2 Yamashiro *et al.* (1999) "Mechanism of the Augmentative Effect of High Polyethylene Glycol (PEG) Concentrations on the Thyroid Stimulating Activity in TSAb-IgG Using a Porcine Thyroid Cell Assay," Endocrine Research 25:67-75.

3. **A long-felt and unsatisfied need in the art for a more accurate assay for detecting thyroid stimulating antibodies was satisfied by the instantly claimed methods**

Despite advances in the art, there remained a need for an assay that more accurately correlated the detection of thyroid stimulating antibodies with clinically diagnosed Graves' disease. The claimed invention solved the long-felt need in the art; 8 of the 10 laboratories in the United States that carry out bioassays for thyroid stimulating antibodies have switched to the instantly claimed methods, and the remaining 2 laboratories are considering switching. It is important to note that because of the technical complexity of the bioassay for thyroid stimulating antibodies, and to the best of my knowledge, the bioassay is performed in the United States by only 10 specialized laboratories. Prior to the introduction of the instantly claimed assay method that utilizes CHO-RLuc cells and PEG, these 10 laboratories used either the FRTL5 cells with the RIA of cAMP or the CHO cells containing the human TSH receptors and the RIA of cAMP. My communications with workers in these laboratories show that 8 of the 10 laboratories that currently offer the bioassay have already converted to, and are currently using, the instantly claimed assay method; the 2 remaining laboratories are considering switching to the instantly claimed assay method.

Based on my experience in the relevant art and on the above, it is my opinion that one of ordinary skill in the art would not have had a reasonable expectation of success in practicing the claimed methods based on the combined teachings of Evans *et al.* and Yamashiro *et al.*

4. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

Dated: May 12, 2004

By: James L. Brown
James L. Brown

# Curriculum Vitae
# of
# James L. Brown

**26 Pleasantview Drive**
**Athens, OH 45701**
**740-594-8522**

## EDUCATION

University of Missouri, Columbia, MO, BS, Biology/Chemistry, 1957.
University of Missouri, Columbia, MO, MS, Physiology/Biochemistry, 1959.
University of Oregon, Eugene, OR, Biochemistry, 1963.

## EMPLOYMENT HISTORY

Nuclear Consultants Corporation, St. Louis, MO, 1963-1966.
Head of R & D and Quality Control.

Mallinckrodt, Inc., St. Louis, MO, 1966-1984.
(Nuclear Consultants was acquired by Mallinckrodt)
Assistant Director of Radiopharmaceutical R & D.
Associate Director of Radiopharmaceutical R & D.
Director of Radiopharmaceutical R & D.

Diagnostic Hybrids, Inc., Athens, OH, 1984-1986.
Director of Product Development.

Binax, Inc., St. Louis, MO, 1986-1988.
Director, Product Development.

Diagnostic Hybrids, Inc. Athens, OH, 1988-Present.
Vice President, New Product Development.
Vice President, New Product Development & Regulatory Affairs.
Senior Vice President & Chief Operating Officer.

## WORK EXPERIENCE

Nuclear Consultants Corporation, Manufacturer of Radiopharmaceuticals.
Responsible for R & D of 19 new *in vitro* and *in vivo* products and at various times, for Manufacturing and QC.

Mallinckrodt, Inc., Manufacturer of Chemicals, X-Ray Contrast Media and Radiopharmaceuticals.
Responsible for R & D of 33 new *in vitro* and *in vivo* products. The work included the use of more than 20 different radioisotopes and quantities >1000 Curies used in nuclear medicine.

Binax, Inc., Manufacturer of *in vitro* Diagnostic Immunoassay Kits.
Responsible for R & D of 4 ImmunoRadioMetric Assays for human hormones and 2 ELISA's for animal use.

Diagnostic Hybrids, Inc., Manufacturer of Cell Culture products, Tests for use in Virology and Thyroid Function Tests.
Responsible for new product development, implementing cGMP, QA and QC methods and procedures and obtaining regulatory approval on new products and cell lines.

**US PATENTS (All with foreign filings.)**

3,655,985: Brown, J.L., Himebaugh, D.T., and Montgomery, J.R. (1972). Radiation-Shielding Receptacle for a Bottle for Receiving a Radioactive Eluate.

3,714,344: Brown, J.L. (1973). Method for Determining Thyroxine in Blood Serum and Reagent Therefor.

3,745,211: Brown, J.L. and Hallett, F.P. (1974). Method for Determining Thyroxine in Serum and Reagent Therefor.

3,830,746: Brown, J.L. and Harris, O. (1974). Method for Preparing Tc-99m Generators Loaded with Fission Product Mo-99.

3,833,509: Brown, J.L. and Harris, O. (1974). Radionuclide Generator Production Method: Tc-99m Radioactive Isotope.

3,966,896: Brown, J.L. and Glovsky, J. (1976). Radioimmunoassay for Plasma Renin Activity: Enzyme Inhibitors.

4,064,227: Brown, J.L. and Lyle, L.R. (1977). Radioimmunoassay Method for the Determination of Cardiotonic Glycosides.

4,210,418: Brown, J.L., Lin, W.H.T. and Woods, J.W. (1980). Container for Immunochemical and Enzymatical Determinations or Procedures.

6,472,206: Scholl, D.R., Ambesi-Impiombato, F.S., Brown, J.L., Kohn, L.B., and Jollick, J.A. (2002). *In Situ* Growth, Freezing and Testing of Cultured Cells.

**PUBLICATIONS**

Thorson, S.C., Tsujikawa, R., Brown, J.L., Morrison, R.T. and McIntosh, H.W. (1970). Evaluation of a Simplified Method for Determining Serum Thyroxine by Competitive Protein Binding Analysis. *Acta Endocrin.*, 64:630-636.

Mincey, E.K., Thorson, S.C. and Brown, J.L. (1971). A new *in vitro* Blood Test for Determining Thyroid Status: The Effective Thyroxine Ratio. *Clin. Biochem.*, 4:286-291.

Mincey, E.K., Thorson, S.C., Brown, J.L., Morrison, R.T. and McIntosh, H.W. (1972). A new Parameter of Thyroid Function: The Effective Thyroxine Ratio. *J. Nuc. Med.*, 13:165-168.

Brown, J.L. (1979). Factors in the Development of an RIA Test System. *Clin. Lab. Prods.*

Swierkosz, E.M., Scholl, D.R., Brown, J.L., Jollick, J.D. and Gleaves, C.A. (1987). Improved DNA Hybridization Method for Detection of Acyclovir-Resistant Herpes Simplex Virus. *Antimicrob. Agents and Chemother.*, 31:1465-1469.